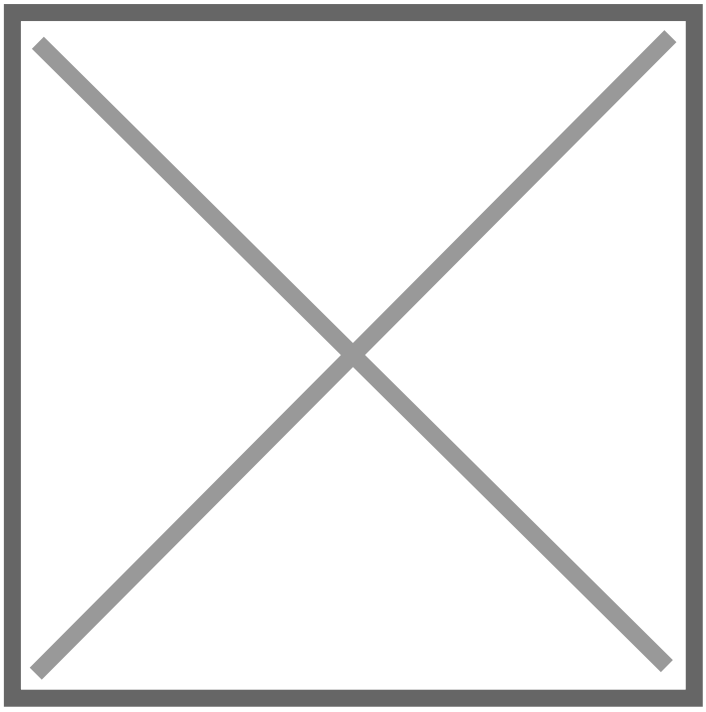
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Drug Discovery in the 21st Century and Beyond

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The inherent screening process for drug molecules could be a potential bottleneck and adopting newer ways can give head start to discover potential new drug molecules.



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Dr Soni is president and COO, Premas Biotech Pvt Ltd and has over 15 years of varied and in-depth experience in the field of biotechnology with significant exposure in recombinant protein expression in bacteria, yeast and mammalian cells, drug discovery research pertaining to cancer, infectious diseases, respiratory and inflammatory disorders.

Drug discovery had its origin in the late 1800s with the isolation and characterization of natural products and their derivatives. The science of drug discovery has come a long way since then with the chemical and biological revolutions aiding the process of drug discovery to make it more rational leading to efficacious and more safer drugs for the benefit of mankind. The last century witnessed major breakthroughs in the field of biological sciences leading to the discovery of DNA structure followed by restriction enzymes that gave birth to recombinant DNA technology leading to the discovery of PCR, inventions that have not only revolutionized the field of biology but also modern day drug discovery.

The protein targets used in the modern drug discovery process has been made possible by cloning and over-expressing these in high quantities for high-throughput screening. The sequencing of the human genome has led us to a plethora of targets that can be exploited for drug discovery in various therapeutic areas, albeit to a limited extent as a number of genes (protein targets) still remain a mystery with regard to their specific functional role they play physiologically. The modern day drugs are divided into chemical entities (small molecule drugs as we all know and call them) and biological entities or bio-therapeutics (proteins that act as drugs).

Although a number of blockbuster drugs are in the market from various global pharmaceutical companies that have aided the medical science in providing cure for a number of diseases, there is always a hunt for novel molecules (be it small molecule or proteins) as patent expiry of branded drugs pave the way for other drug companies to bring forth generic versions of the branded drugs

A current assessment of the drug discovery space reveals that there is a dearth of novel drug molecules and pharmaceutical companies are fighting an incessant battle to bring forward new potential drugs to the market. The reasons for that are manifold and this review does not warrant discussing those here. However, I am confident enough that the drug czars would agree to the school of thought that the inherent screening process for drug molecules could be a potential bottleneck. The current screening process revolves around analyzing the structure/structural homologues of the molecule(s) and then screening them for appropriate function(s). An immense amount of capital investment has already been made by global pharmaceutical companies in high-throughput and ultra high-throughput screening platform with a little success. So what does one do? Should we change the paradigm of hunting for novel molecules? What is that change and how that would benefit the field? We really need to think "out of the box" to answer these questions.

One of the ways is to identify the functional aspect of the potential drug in the first place rather than its structure. This could lead us to molecules with novel structures that have already been shown to be efficacious on the appropriate assay. What that entails is that companies (contract research as well as pharmaceutical companies) should focus on designing and validating functional screening assays to assess the potency of small molecules and proteins. Once proven efficacious, one can delineate the structure and perform optimization studies to proceed further. This approach can give a head start to discover potential new drug molecules and provide pharmaceutical companies a much needed shot in the arm to improve pipeline of future drugs.

Premas Biotech has forayed into this area by developing Functional Genomics Technology (FGT) assays for lead identification, currently focusing on the therapeutic areas of Central Nervous System, Aging and Oncology. This rational "function-to-structure" approach has generated considerable interest among global pharmaceutical majors and is currently being validated for proof of concept studies. The FGT entails the generation of a multi-dimensional proteo-genomic ecosystem that evaluates the efficacy of a potential therapeutic drug based on its functional aspects rather than the structure and has the potential to revolutionize the drug discovery process by changing the current paradigm for screening novel therapeutics. These FGT assays will soon be available for the drug discovery industry for screening purposes.

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